## REMARKS

Reconsideration is requested.

Claims 1-19 have been canceled, without prejudice.

Claims 20-22 have been added and are pending. No new matter has been added. Support for the amended claims may be found, for example, on page 7, fourth paragraph (stringency conditions), page 5, line 6 (percent identity) and now-canceled claim 9 (¶(a) of claim 20). No new matter has been added.

The specification has been amended to include the attached Abstract, in response to the Examiner's comment in paragraph 2A. of page 2 of the Office Action dated May 10, 2004.

The specification has been amended to include a cross-reference to the parent PCT application , in response to the Examiner's comment in paragraph 2B. of page 2 of the Office Action dated May 10, 2004.

The Section 101 rejection of claims 8-10 is moot in view of the above. The claims are submitted to define patentable subject matter and consideration of the following in this regard is requested.

The Examiner is understood to have believed that the utility of the subject matter of the now-canceled claims is derived solely from information based on structural similarity with other proteins and that it has not been shown that the protein encoded for by SEQ ID NO: 3-17 is a human sodium channel. The Examiner is requested to advise the undersigned in the event the applicants have misunderstood the Examiner's basis of the Section 101 rejection.

The specification describes, in the introduction, that various voltage-gated sodium channels were known before the priority date of the present application. The known voltage-gated sodium channels had been classified as TTX-sensitive and TTX-resistant, as set out at page 2, lines 1 to 5 of the specification. Most known voltage-gated sodium channels were TTX-sensitive channels and they were known to be located mostly in the central nervous system. Two channels had been found which were inhibited only by micromolar concentrations of TTX (ie "TTX resistant"). They were the major cardiac channel and the sensory neurone specific channel (SNS/PN3).

The present inventors have discovered a new channel with some similarities to the known SNS channel. However, in addition to the sequence similarity information set out at page 3, final paragraph, the present inventors have carried out various experiments that demonstrate the utility of the channel. Some of those experiments were carried out using the rat $SNS_{2a}$ and others were carried out using the human $SNS_{2a}$ sequence. The rat $SNS_{2a}$ sequence is set out in SEQ ID NO 1; the majority of the human $SNS_{2a}$ sequence is set out in sequences SEQ ID NO 3-17, as shown in Figure 2.

It was demonstrated that the peptides of the invention are sodium channels and that they are TTX-resistant. Specifically, at page 25, line 3 to page 27, line 9, electrophysiology experiments are described. The results of those experiments are shown in Figure 11. In the experiments, it was shown that the rat $SNS_{2a}$ channel is a voltage-gated sodium channel. Transient inward currents were evoked by membrane depolarisation at potentials positive to -70mV, peaking at -20mV and being reversed

close to the Na+ equilibrium potential. The currents were found to be highly resistant to TTX, the estimated IC50 value being 1mM (page 26, line 15).

Further, it was demonstrated that the sodium channels of the invention are present in small diameter cell bodies of peripheral sensory neurons. Antibodies were raised against the terminal portions of the channel (amino acid residues 2 to 15 and 1748 to 1765) and a riboprobe was used that incorporated the 18/14 sequence as indicated in Figure 1). The immunohistochemistry and riboprobe experiments demonstrating the localization of the channels in rat DRG sections are described at page 23, second paragraph of the application.

The antibody raised against rat $SNS_{2a}$ cross reacted with the human $SNS_{2a}$ as set out on page 24, lines 1 to 3. It was then shown that the human $SNS_{2a}$ channel is located only in small diameter neuronal cell bodies.

It is submitted that the close sequence similarity between the human $SNS_{2a}$ and the rat $SNS_{2a}$ (>80 %) and the fact that they are expressed in the same tissues in the two species very strongly shows the skilled person that the human sequence also codes for a voltage-gated sodium channel. That conclusion is based on experimental evidence, not mere inference from database comparisons.

Furthermore, as set out at page 2, second paragraph of the application, small diameter neurones of mammalian dorsal root ganglion cells were known to be involved in the transmission of pain impulses. It was also known that anaesthetic, anticonsulsant and antiarrythmic drugs that have sodium channel blocking activity have analgesic effects (page 3, first full paragraph). The fact that the sodium channel of the invention is TTX-resistant and found only in the small diameter neurones of mammalian dorsal root

ganglion cells strongly suggests to the person of ordinary skill in the art that the sodium channels of the invention have utility as targets for the screening of agents that will be active in inhibiting the channel and hence in inhibiting pain transmission.

It is accordingly submitted that it has been shown that the claimed sequences have several real, substantial and credible utilities: they have been shown to be voltage-gated sodium channels and they have been strongly indicated to be involved in pain transmission and thus have utility in the discovery of agents that mediate pain transmission.

The claims are submitted to define patentable subject matter.

The Section 112, first paragraph "enablement", rejection of claims 8-10 is moot in view of the above. The claims are submitted to be supported by an enabling disclosure and consideration of the following in this regard is requested.

The claims recite specific stringent hybridization conditions and require that all of the sequences as defined in SEQ ID 3 to 17 wherein ascending numerical order represents the order in which the SEQ ID is read in the 5' to 3'. It is submitted that nucleic acids that have the sequences now claimed provide a channel that is operative without undue experimentation being necessary.

The ordinarily skill person is well acquainted with methods for generating DNA sequences, such as by site-directed mutagenesis, which will meet the claimed identity requirement and not require an undue amount of experimentation to make and/or use. Once a sequence of the claims has been prepared, the ordinarily skilled person is able to determine whether the sequence has the noted properties of the invention, again without an undue amount of experimentation.

The claims are submitted to be supported by an enabling disclosure.

The Section 112, first paragraph "written description", rejection of claims 8-10 is moot in view of the above. The claims are submitted to be adequately described in the specification, as indicated above.

The Section 102 rejections of claims 8 and 10 stated on pages 8-10 of the Office Action dated May 10, 2004, are moot in view of the above.

The claims are submitted to be patentable over the cited art as, for example, the sequence of paragraphs (a)-(e) of claim 20 are not taught or suggested by the cited art.

Specifically, the claims require, for example, in paragraph (a) of claim 20 that all of the sequences as defined in SEQ ID NOs: 3 to 17 be present wherein ascending numerical order represents the order in which the SEQ ID NO: is read in the 5' to 3'. It is submitted that none of the cited art discloses a polynucleotide of the claimed invention. While there may be a teaching in the art of short portions of the claimed polynucleotide, the applicants submit that such portions do not amount to 85% of the total length of the nucleotide comprising all of the sequences as defined in SEQ ID NOs:3 to 17 wherein ascending numerical order represents the order in which the SEQ ID NO: is read in the 5' to 3', as claimed. The claims are submitted to be patentable over the cited art.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned in the event anything further is required.

Respectfully submitted,

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